

PATENT COOPERATION TREATY

WO 99/25728
PCT/US98/24273

OP: FCC
G: PAUNSON

PCT

From the INTERNATIONAL BUREAU

NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

To:

CONSALVI, Mary, S.
Lyon & Lyon LLP
Suite 4700
633 West Fifth Street
Los Angeles, CA 90071
ÉTATS-UNIS D'AMÉRIQUE

Date of mailing (day/month/year) 27 May 1999 (27.05.99)		IMPORTANT NOTICE	
Applicant's or agent's file reference 238/087-PCT			
International application No. PCT/US98/24273	International filing date (day/month/year) 13 November 1998 (13.11.98)	Priority date (day/month/year) 14 November 1997 (14.11.97)	
Applicant AMYLIN PHARMACEUTICALS, INC. et al			

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:
AU,CN,EP,IL,JP,KP,KR,US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:

AL,AM,AP,AT,AZ,BA,BB,BG,BR,BY,CA,CH,CU,CZ,DE,DK,EA,EE,ES,FI,GB,GE,GH,GM,HR,HU,ID,
IS,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MD,MG,MK,MN,MW,MX,NO,NZ,OA,PL,PT,RO,RU,SD,SE,SG,
SI,SK,SL,TJ,TM,TR,TT,UA,UG,UZ,VN,YU,ZW

The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on
27 May 1999 (27.05.99) under No. WO 99/25728

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the national phase, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer J. Zahra
Facsimile No. (41-22) 740.14.35	Telephone No. (41-22) 338.83.38

JUN 14 1999

S.D. PROSECUTION

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark
Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year)

22 June 1999 (22.06.99)

International application No.

PCT/US98/24273

Applicant's or agent's file reference

238/087-PCT

International filing date (day/month/year)

13 November 1998 (13.11.98)

Priority date (day/month/year)

14 November 1997 (14.11.97)

Applicant

BEELEY, Nigel, Robert, Arnold et al

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

28 May 1999 (28.05.99)



in a notice effecting later election filed with the International Bureau on:

2. The election



was



was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Sean Taylor

Telephone No.: (41-22) 338.83.38

gr

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WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C07K 7/00, A61K 38/00		A1	(11) International Publication Number: WO 99/25728
			(43) International Publication Date: 27 May 1999 (27.05.99)
(21) International Application Number: PCT/US98/24273 (22) International Filing Date: 13 November 1998 (13.11.98) (30) Priority Data: 60/066,029 14 November 1997 (14.11.97) US (71) Applicant (for all designated States except US): AMYLIN PHARMACEUTICALS, INC. [US/US]; 9373 Towne Centre Drive, San Diego, CA 92121 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): BEELEY, Nigel, Robert, Arnold [US/US]; 227 Loma Corta Drive, Solana Beach, CA 92131 (US). PRICKETT, Kathryn, S. [US/US]; 7612 Trailbrush Terrace, San Diego, CA 92126 (US). (74) Agents: CONSALVI, Mary, S. et al.; Lyon & Lyon LLP, Suite 4700, 633 West Fifth Street, Los Angeles, CA 90071 (US).			(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
(54) Title: NOVEL EXENDIN AGONIST COMPOUNDS			
(57) Abstract Novel exendin agonist compounds are provided. These compounds are useful in treating diabetes and conditions which would be benefited by lowering plasma glucose or delaying and/or slowing gastric emptying.			

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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EE	Estonia						

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/24273

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : C07K 7/00; A61K 38/00

US CL : 530/324, 855, 856; 514/12, 866

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 530/324, 855, 856; 514/12, 866

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
none

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

STN/reg
exendin, diabetes, registry sequence search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 5,424,286 A (ENG) 13 June 1995, see entire document, especially the abstract; column 2, lines 37-60; columns 9-14.	1-29, 31-70, 72, 73

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	* T	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
* A		
document defining the general state of the art which is not considered to be of particular relevance	* X	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
* E		
earlier document published on or after the international filing date	* Y	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
* L		
document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	* G	document member of the same patent family
* O		
document referring to an oral disclosure, use, exhibition or other means		
* P		
document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

18 MARCH 1999

Date of mailing of the international search report

30 MAR 1999

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

Cybille D-Muirheid

Telephone No. (703) 308-0196

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/24273

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 30 and 71
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

No meaningful search could be carried for the SEQ ID NO:s in claims 30 and 71 because the CRF for the case is defective.

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

REC'D 20 MAR 2000

WIPO

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(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 238/087-PCT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US98/24273	International filing date (day/month/year) 13 NOVEMBER 1998	Priority date (day/month/year) 14 NOVEMBER 1997
International Patent Classification (IPC) or national classification and IPC IPC(6): C07K 7/00; A61K 38/00 and US Cl.: 530/324, 855, 856; 514/12, 866		
Applicant AMYLIN PHARMACEUTICAL, INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 10 sheets.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 28 MAY 1999	Date of completion of this report 23 FEBRUARY 2000
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized Officer <i>Cybil D-Muirheid</i> Cybil D-Muirheid
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US98/24273

I. Basis of the report

1. This report has been drawn on the basis of *(Substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments)*:

☒ the international application as originally filed.

☒ the description, pages 1-115 , as originally filed.

pages NONE , filed with the demand.

pages NONE , filed with the letter of _____.

pages _____ , filed with the letter of _____.

☒ the claims, Nos. 1-73 , as originally filed.

Nos. NONE , as amended under Article 19.

Nos. NONE , filed with the demand.

Nos. NONE , filed with the letter of _____.

Nos. _____ , filed with the letter of _____.

☒ the drawings, sheets/fig 1-11 , as originally filed.

sheets/fig NONE , filed with the demand.

sheets/fig NONE , filed with the letter of _____.

sheets/fig _____ , filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

☒ the description, pages none .

☒ the claims, Nos. none .

☒ the drawings, sheets/fig none .

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the ~~Supplemental Box~~ Additional observations below (Rule 70.2(c)).

4. Additional observations, if necessary:

NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US98/24273

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application.

☒ claims Nos. 30 and 71

because:

☐ the said international application, or the said claim Nos. _ relate to the following subject matter which does not require international preliminary examination (*specify*).

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _ are so unclear that no meaningful opinion could be formed (*specify*).

☐ the claims, or said claims Nos. _ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 30 and 71.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US98/24273

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. STATEMENT**

Novelty (N)	Claims	<u>(Please See supplemental sheet)</u>	YES
	Claims	<u>(Please See supplemental sheet)</u>	NO
Inventive Step (IS)	Claims	<u>(Please See supplemental sheet)</u>	YES
	Claims	<u>(Please See supplemental sheet)</u>	NO
Industrial Applicability (IA)	Claims	<u>(Please See supplemental sheet)</u>	YES
	Claims	<u>(Please See supplemental sheet)</u>	NO

2. CITATIONS AND EXPLANATIONS

Claims 1, 2, 5-8, 15-27, 29, 31-44, 46, 48-49, 56-69, 72 lack novelty under PCT Article 33(2) as being anticipated by ENG 5,424,286.

ENG discloses pharmaceutical compositions of exendin-3 and exendin-4 or derivatives thereof, wherein the SEQ ID NO's: 1-7, disclosed at columns 9-13, read on the claimed sequences.

ENG further discloses that the peptides and pharmaceutical compositions thereof are useful in treating diabetes mellitus and hyperglycemia. The compositions may be administered intravenously, intramuscularly, subcutaneously or intraperitoneally at dosages of 0.1 pg/kg to 1,000 mg/kg body weight. Please see column 5, lines 13-19.

Claims 1, 2, 5-8, 11-12, 15-27, 28, 29, 31-44, 46, 48-49, 52-53, 56-69, 72 lack an inventive step under PCT Article 33(3) as being obvious over ENG, supra.

ENG as disclosed above.

ENG does not disclose that position 4 may be substituted with an Ala residue, however, substitution of Gly with an Ala is obvious and well within the capability of the skilled artisan in view of the fact that Gly and Ala are homologous amino acids and that substitution of one with the other would not expect to change the activity of the peptides.

Claims 1-29, 31-70, 72-73 meet the criteria set out in PCT Article 33(4), because the claimed invention can be used in industry.

Claims 3, 4, 9-10, 13, 14, 28, 45, 47, 50-51, 54, 55, 70, 73 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest Applicant's claimed peptide sequences.

_____ NEW CITATIONS _____

NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US98/24273

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

Claims 1, 29, 42 are objected to under PCT Rule 66.2(a)(iii) as containing the following defect(s) in the form or contents thereof:
In claims 1, 29 and 42 amino acid substituents "Xaa₁₇"-"Xaa₂₃" are misnumbered.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US98/24273

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

V. 1. REASONED STATEMENTS:

The report as to Novelty was positive (YES) with respect to claims 3, 4, 9-12, 13, 14, 28, 45, 47, 50-53, 54, 55, 70, 73.

The report as to Novelty was negative (NO) with respect to claims 1, 2, 5-8, 15-27, 29, 31-44, 46, 48-49, 56-69, 72.

The report as to Inventive Step was positive (YES) with respect to claims 3, 4, 9-10, 13, 14, 28, 45, 47, 50-51, 54, 55, 70, 73.

The report as to Inventive Step was negative (NO) with respect to claims 1, 2, 5-8, 11-12, 15-27, 29, 31-44, 46, 48-49, 52-53, 56-69, 72.

The report as to Industrial Applicability was positive (YES) with respect to claims 1-29, 31-70, 72-73.

The report as to Industrial Applicability was negative (NO) with respect to claims none.